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ENVIRONMENTAL CANCER

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National Cancer Institute
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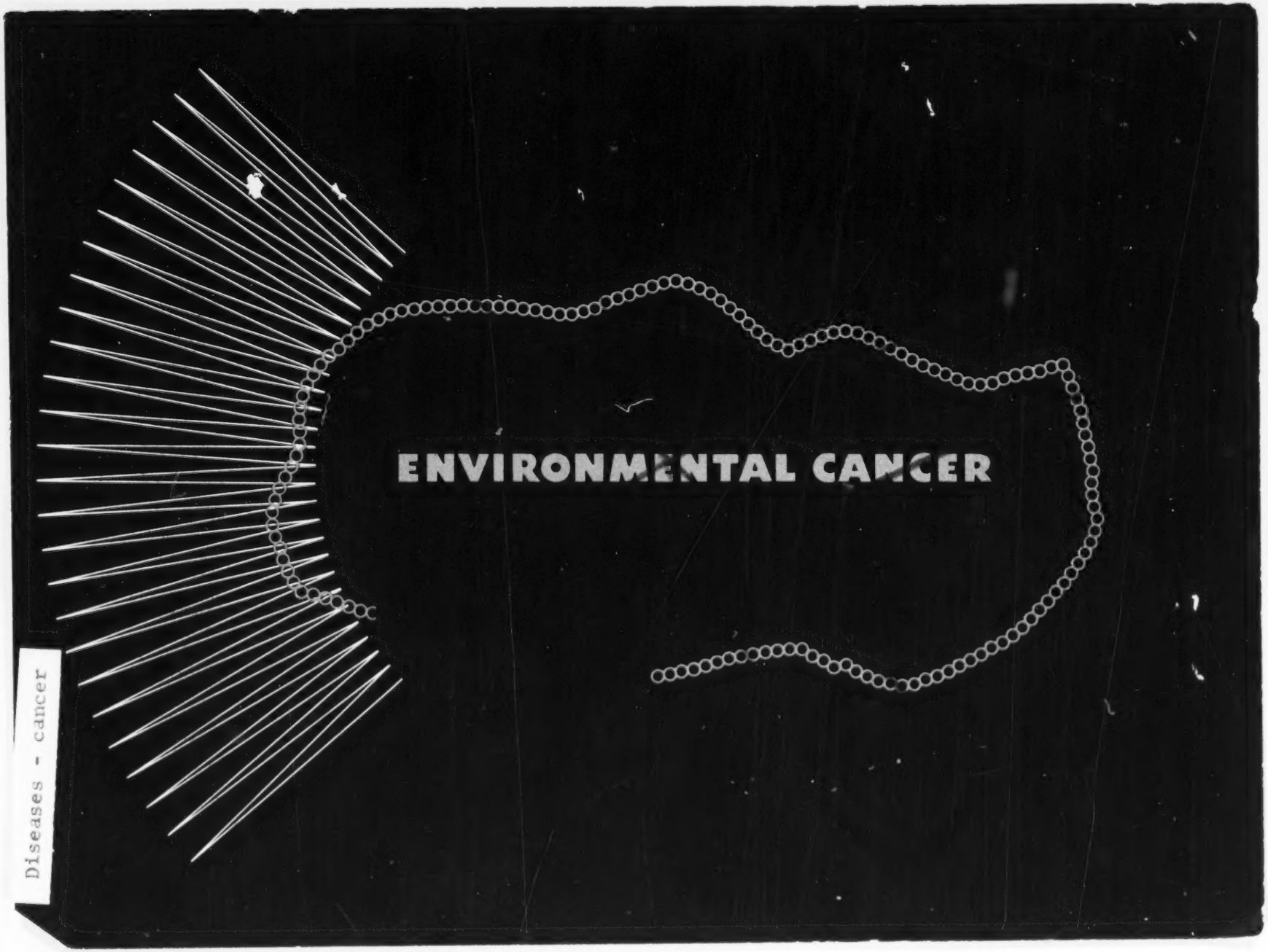

Diseases - cancer

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ENVIRONMENTAL CANCER

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CANCER CONTROL BRANCH, NATIONAL CANCER INSTITUTE

INTRODUCTION

As long as man has existed, his surroundings have been at once his chief support and his chief enemy. The human being is not an independent organism, imposed upon an existing environment. He is, rather, an inseparable part of it. He grew with it and out of it; he always depends on it; and he never can escape it. But to some extent he can control his environment. Where it is harmful, he should do so.

In relatively modern times, the industrial activities of man have added a number of entirely new artificial factors to his natural environment. Many of them contribute to the comfort and the pleasures of life. Yet in the process of their manufacture and use a whole new spectrum of environmental "poisons" has been added to the hazards with which mankind has to contend.

Some of these poisons act obviously and swiftly, and can be controlled because of their very violence. Others pursue a slow, nearly imperceptible course, and exhibit their virulence in end-results which often seem to bear no relation to their origins. Of these, many cause a gradual wastage of the individual organism by means of direct poisoning; others result in chaotic cell growths, arising after a lengthy latent period, and causing a sudden and sometimes inexplicable illness which, unless discovered at an early stage, usually results in death. It is with these latter effects of an industrial civilization that we are concerned—the effects known as environmental cancers.

The destructive growth of undifferentiated body cells which is known as cancer has been a recognized medical problem since eight hundred years before the birth of Christ. In the library of Nineveh there was an inscription, dating from about that time, which described a carcinoma of the breast.

But it was not until the sudden, explosive growth of Western technology,

toward the end of the last century, that medical science obtained the tools necessary for a concentrated attack upon human disease. Because of their more dramatically obvious lethal nature, endemic parasitical ailments came under medical scrutiny before most other types of illness; and these contagious diseases have for the most part fallen before the organized technical onslaught of modern medicine.

But now we are on the threshold of one of the greatest of all battles of man against his environment: the battle against cancer. Today, less than one percent of all cancers have a known or even a suspected cause. Yet this etiologic fraction of one percent is the first wedge of knowledge into a heretofore impenetrable mystery, achieved after an enormous expenditure of time, research, intelligence, and money. That specialists in cancer have been able to identify even this small part of the causes of cancer is as great a step forward, in some ways, as was the discovery of the first pathogenic microorganisms that led to the subsequent conquest of many of the most dangerous infectious diseases.

With few exceptions, the causes of cancer thus far discovered have been found to be of external origin. While this by no means permits the conclusion that all cancers are of exogenous causation, it does indicate that further research may well uncover many more external—*and therefore controllable*—cancerigenic agents.

But the knowledge of a cause in medicine, and control of such a cause, are two completely different elements of this science. The first rarely if ever leads automatically to the second; and the second involves a much wider variety of human activity. It includes, in addition to the purely medical aspects, the planning, coordination and carrying out of a Nation-wide program of remedial legislation, medical education, labor and management supervision, public health controls, and citizen indoctrination.

It is the purpose of this pamphlet to present in brief form the known and suspected environmental causes of cancer, the sources from which they arise, the methods whereby they are discovered, and their carcinogenic dangers are demonstrated, and the programs of control which are essential if these causes of cancer are to be eliminated or at least greatly reduced in potency.

CAUSATIVE FACTORS

The human being may be exposed to one or more of the known or suspected external cancer-producing agents in a variety of ways. Medicinal preparations and devices, dietary deficiences, certain habits, and a few of the environmental factors, all offer some cancerigenic hazards; but the greatest number of known carcinogens are found in connection with man's occupational activities.

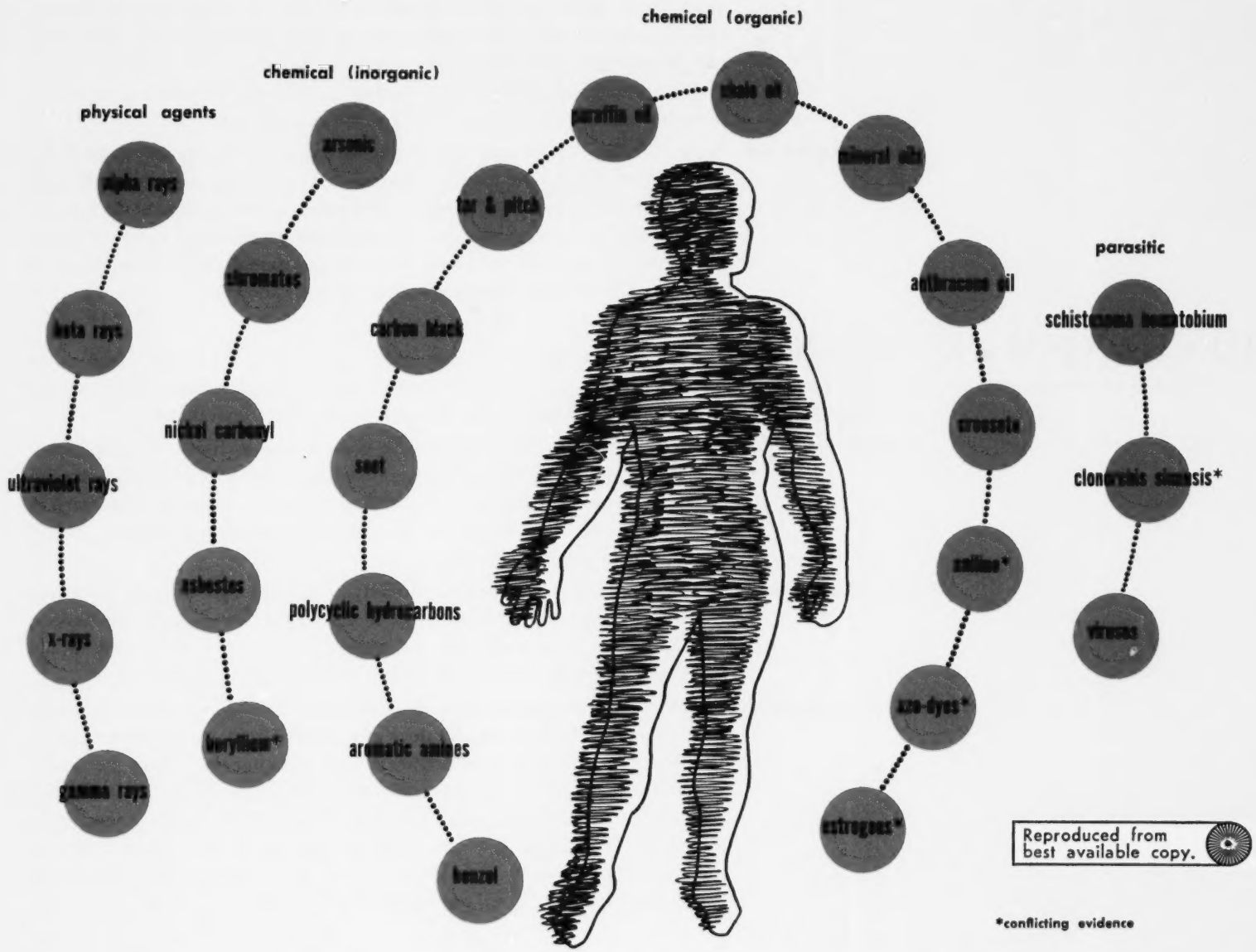
medicine In the medical field, preparations containing arsenicals and coal tar have been known to cause cancer of the skin. Medicinal exposure to X-rays and radium, in the treatment of often nonmalignant diseases, has resulted in cancers of the irradiated tissues in some patients.

diet Dietary deficiencies, particularly of proteins and vitamin B factors, are thought to be responsible for the excessive incidence of cancer of the liver among African Negroes and the inhabitants of Java. Thyroid cancers seem to be related to the occurrence of endemic goiter in population groups suffering from a dietary iodine deficiency.

habits Although there is no definite evidence that tobacco is carcinogenic when smoked or chewed, there is an abnormal incidence of cancer of the mouth in India and the Philippines, where the people chew tobacco-betel nut quids, or place tobacco-lime quids in the groove behind the lower lip. Mouth cancers are also unusually frequent in a certain tribe in India which smokes cigars with the lighted end in the mouth, and thus contracts frequent burns, as well as a concentrated dosage of tobacco tars.

environment, natural The natural environment contains only a few recognized carcinogens. Of these, solar radiation is one of the best proved, particularly as it affects light-skinned people who become overexposed for long periods of time to the carcinogenic ultraviolet radiation in southern dry and sunny climates. An abnormally high arsenic content in drinking water has been shown to cause cancer of the skin and of the internal organs. Infections with the parasite Schistosoma hematobium, common among the fellahs of Egypt, are apparently related to the high incidence of cancer of the bladder found there.

environment, artificial In the artificial environment which has been created by our industrial civilization, soot and certain waste products from the fractionation and distillation


chemical (organic)
chemical (inorganic)
physical agents
parasitic
arsenic
alpha rays
shale oil
paraffin oil
mineral oils
tar & pitch
chromates
anthracene oil
carbon black
beta rays
creosote
nickel carbonyl
soot
ultraviolet rays
aniline*
asbestos
polycyclic hydrocarbons
x-rays
azo-dyes*
beryllium*
aromatic amines
gamma rays
estrogens*
benzol
virosas
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of coal and petroleum, including shale oil, have carcinogenic potentialities. Likewise the wastes resulting from the smelting and processing of certain metals may give carcinogenic properties to the air, water, and soil within the "fume zone" of plants producing them. All types of radioactive emanations are similarly dangerous in the general environment.

occupations

But it is in the occupational activities of an industrial society that most of the carcinogenic dangers are found. Here workers come into close and prolonged contact with substances which either have never before existed in the natural environment, or have existed in such weak concentrations as to be relatively harmless. A chart of the major known occupational carcinogens, some of which are also active in other connections, appears herewith.

MECHANISM OF ACTION

The known or suspected extrinsic carcinogens act on the human organism in one of three different ways. Some carcinogens *directly* cause cancer, among them the aromatic amines, tar, mineral oils, and their derivatives.

direct primary

indirect primary

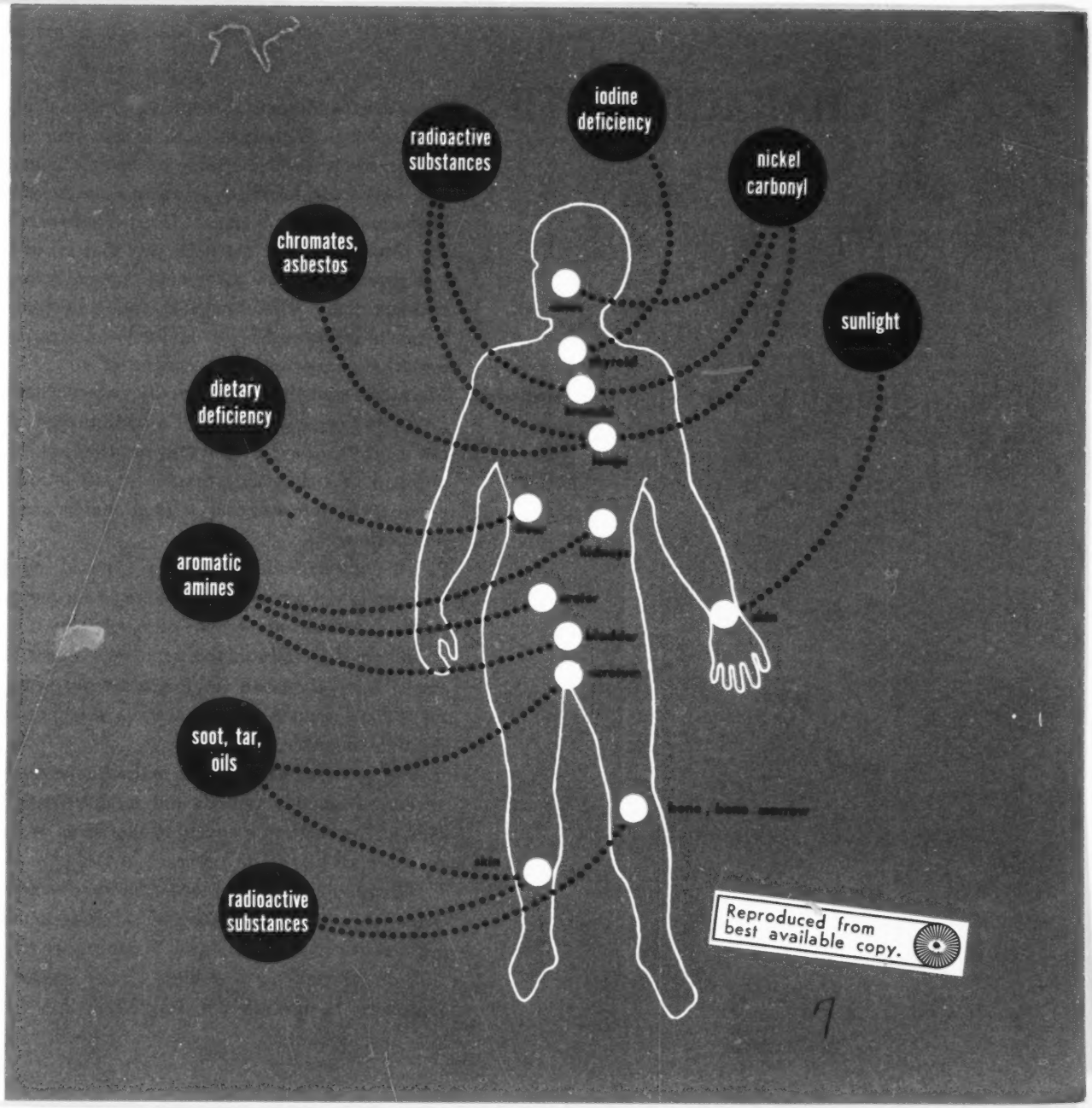
Other agents coming in contact with certain human tissues seem to elicit cancers by producing endogenous carcinogenic substances within the exposed tissues. These comprise all the physical rays and radiations, and certain metals or metallic compounds, including arsenicals, chromates, nickel carbonyl, and possibly asbestos.

indirect secondary

A third group acts even more indirectly. The azo dyes and the suspected chlorinated aliphated hydrocarbons, along with a few dietary imbalances, are thought to cause metabolic disturbances in certain organs, such as the liver, which in turn result in the formation of endogenous carcinogens.

routes of exposure

All of these carcinogens may act through one or more of the following routes of exposure: skin contact, respiratory contact, ingestion, and parenteral introduction. For example, radioactives may cause skin cancer when the skin is overly exposed to them; lung cancer when radioactive emanations and dusts are inhaled; and leukemic manifestations, which are a sort of cancer, when the system is subjected to a very slight but prolonged contact with electronic energy. Bone cancers may also be caused by the ingestion of radioactive substances, or by medicinal overexposure to X-rays.


iodine deficiency
radioactive substances
nickel carbonyl
chromates, asbestos
sunlight
dietary deficiency
aromatic amines
soot, tar, oils
radioactive substances
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CHARACTERISTICS

There are a number of statistical and clinical characteristics of environmental cancers which are helpful in their discovery and evaluation. Some apply to the cancers themselves; some to the carcinogens. While not always significant when considered singly, these characteristics when fitted together tend to form a pattern that is typical for environmental carcinogenesis.

Moreover, it is not necessary that all of these characteristics be found in a given group or a given environment before an environmental origin can be suspected. It usually is essential, however, that one or the other of the elements mentioned below under Point One be presented before an environmental etiology can be prognosticated.

statistical

The major statistical characteristics of environmental cancers follow:

1. An excessive incidence of a certain type of cancer among members of a given occupational group suggests the existence of an environmental carcinogen. Likewise, the presence of an industry using known or suspected carcinogens indicates that occupational cancers may be found in the working population.
2. The rate of incidence among exposed individuals, and the length of the average latent period found, depend on the potency of the carcinogen and on the duration and intensity of exposure to it.
3. Where a racially mixed population exists, these relations are modified in regard to solar cancers and to cancers caused by mineral oils and tar products, since dark-skinned peoples are less susceptible to such carcinogens than are the light-skinned groups.
4. Age at onset of exposure and average length of latent period determine within reasonable bounds the manifestation age of occupational cancer. Neither heredity nor advanced age seem to have any appreciable influence on susceptibility to or incidence of this type of malignant tumor.
5. Occupational cancers occur predominantly in males, since more males come in contact with industrial carcinogens than do females. The existing differences in sex distribution of cancer are in general a reflection of this fact, and do not indicate that there is any special susceptibility to occupational cancer on the part of the male sex.

clinical There are three major clinical factors which characterize environmental cancers:

1. The site of exogenously caused cancers in the body depends on the physical and chemical properties of the carcinogen, and on the type, intensity, and duration of exposure to it. Many such cancers develop at the point where the carcinogen exerts the most intense and prolonged action, regardless of the original route of primary contact with it. With skin cancers the contact route and the site are usually identical, but with internal cancers they often differ.
2. A high rate of primary multiplicity, or of two or more simultaneous cancers not caused by metastasis, is characteristic of occupational cancer, and is the result of the action of a potent carcinogen and of an intense and long-continued exposure to it.
3. Characteristic occupational lesions, such as arsenic and tar dermatoses, actinic dermatitis, and radiation osteitis, are precancerous warnings of occupational cancers to come.

CANCER AND INDUSTRY

The most significant part of the environmental cancer problem is its occupational aspect. Fully 90 percent of the known environmental carcinogens never existed in dangerous concentrations until industrial processes brought workers into constant and close contact with them.

radioactive substances The growth of recognized exogenous cancers parallels in startling fashion the growth of those industries and professions in which extrinsic carcinogens are a factor. One of the most obvious is the mining, manufacture, and use of radioactive materials, and the use of X-ray apparatus. It is estimated that 50 percent of the uranium miners at Joachimsthal, in Czechoslovakia, and up to 80 percent of the cobalt miners in the radioactive mines at Schneeberg, die of lung cancer, most probably as a result of radioactive poisons. From the first recorded appearance of a recognized X-ray cancer in 1902, the spread of radiation cancers has automatically followed new developments and new uses of these dangerous materials and instruments. A case in point is the

environmental carcinogens

NAME	DATE	DISCOVERER	ORGANS AFFECTED	NATURE OF EXPOSURE*
SOOT	1775	Pott	Skin (scrotum)	Occ. (chimney sweeps)
ARSENIC	1822	Ayrton	Skin	Occ., env.
PARAFFIN OIL	1875	Volkmann	Skin	Occ. (lignite & shale oil indust)
SHALE OIL	1876	Bell	Skin	Occ.
PITCH & TAR	1876	Manouvriez	Skin	Occ.
CRUDE OILS (SOME)	1879	Härting & Hesse	Skin	Occ.
SUN (ULTRAVIOLET)	1893	Unna	Skin	Occ. (farmers, sailors)
AROMATIC AMINES	1895	Rehn	Bladder	Occ. (dye industry)
ROENTGEN RAYS	1902	Frieben	Skin	Occ., med.
SCHISTOSOMA HEMATOBIUM	1911	Ferguson	Bladder	Env., occ. (Egypt)
ROENTGEN RAYS, RADIUM	1911	Von Jagicz, Schwartz & Von Siebenrock	Bone marrow (leukemia)	Occ., med.
ANTHRACENE OIL	1913	Rambousek	Skin	Occ.
BETEL NUT, TOBACCO	1915	Davis	Mouth	Habit (India, Malay)
DIET DEFICIENCY	1919	Mouchet & Gerard	Liver	Env. (poverty diets, Africans, Chinese)
RADIUM	1920	Leitch & Sequira	Skin	Occ. and med.
LUBRICATING OILS	1922	Southam & Wilson	Skin	Occ. (mule spinners)
CREOSOTE	1924	Cookson	Skin	Occ.
BENZOL	1928	Delore & Bergamo	Bone marrow (leukemia)	Occ.
URANIUM	1929	Löwy	Lung	Occ.
RADIOACTIVE RAYS	1931	Martland	Bone	Occ. & med.
CHROMATES	1932	Alwens	Lung	Occ.
NICKEL CARBONYL	1932	Stephens	Nasal sinuses, lung	Occ.
ASBESTOS	1934	Wood & Gloyne	Lung	Occ.
RADIOACTIVE RAYS	1934	Neitzel	Lung	Occ. & med.
TAR FUMES	1936	Kahawata	Lung	Occ.

*occ—occupational
env—environmental
med—medicinal

tragedy of the luminous dial painters in the United States, many of whom have, since 1928, died of bone cancers resulting from their habit of wetting the radioactive paint brushes with their lips.

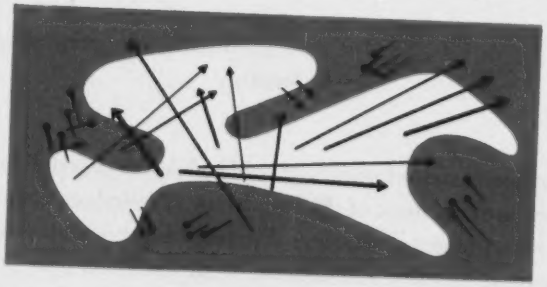
dyes Similarly, bladder cancers resulting from appreciable exposure to certain dye intermediates have closely followed the establishment of industries making or using these chemicals. In almost every case the elapsed time between the first possible exposure and the recognized appearance of the cancers has borne a direct relation to the known average latent period for the development of such lesions.

The following timetable of first reports of occupational cancers shows how closely they are related to the original establishment of the industries producing or using the carcinogens involved.

FUTURE OCCUPATIONAL CANCER HAZARDS

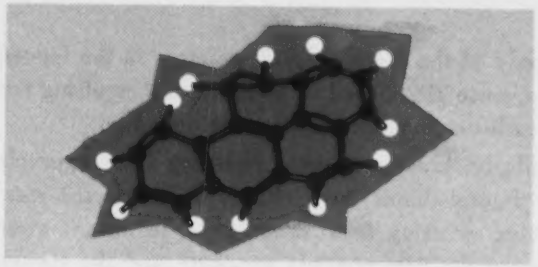
It is obvious that the environmental cancer spectrum is only partially known. New carcinogens are discovered from time to time, and undoubtedly will continue to be.

The most dangerous areas in our modern environment, from the point of view of future cancer hazards, are the following:



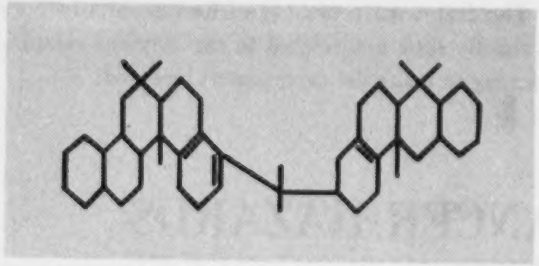
radioactive substances

1. The field of radioactive substances—uses, scientific, medical, industrial, and military—wherever radiations obtained from radioactive materials, from X-rays, or from other sources, come in contact with the human being.



chemicals

2. The whole area of hydrocarbon and metallurgic research and development. This includes the high-temperature distillation and fractionation of petroleum, the production and processing of shale oil, bitumen, and coal by recently developed methods of cracking and hydrogenation, and the manufacture of new organic chemicals from these substances.



synthetic chemicals

3. More generally, the wide field of organic chemistry, which is developing thousands of new synthetic chemicals often without adequate testing for cancer-producing properties. These, as well as the other chemicals, are entering our environment through an enormous number of routes, many of which may subject workers or users to dangerous concentrations of now-unknown carcinogens. Such materials are becoming increasingly common in industry; in agriculture as insecticides and synthetic fertilizers; and in medicines, prepared foods, and cosmetics, all designed for direct personal use and consequently all presenting possible carcinogenic hazards.

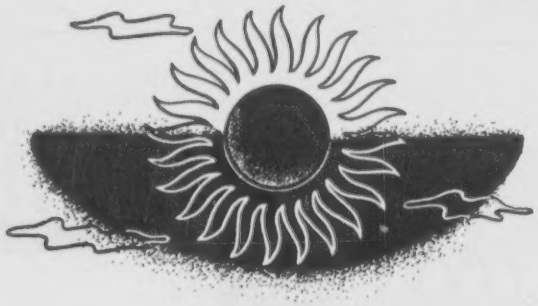
EPIDEMIOLOGY

The two basic techniques of medical research, epidemiology and experimentation, provide most of the important knowledge on the existence and incidence of environmental cancer. Epidemiological studies of such cancers are among the most complex and difficult of all statistical operations, because of the great number of special factors which enter each project.

The epidemiology of environmental cancer falls into two major divisions: general population studies on regional, racial, sex and other very broad bases; and special population studies, either community, industrial plant, or tribal, usually in relation to some suspected carcinogen.

solar cancer

Significant results on the relation of solar cancers to intensity and duration of sunlight have been obtained from the first, generalized type of study. The chart of skin cancer incidence in certain United States cities shows important variations in proportion to differences in total annual solar radiation. Generalized studies of this type are usually based on already existing disease incidence figures, such as those published by the *Public Health Service* of the *Federal Security Agency*.

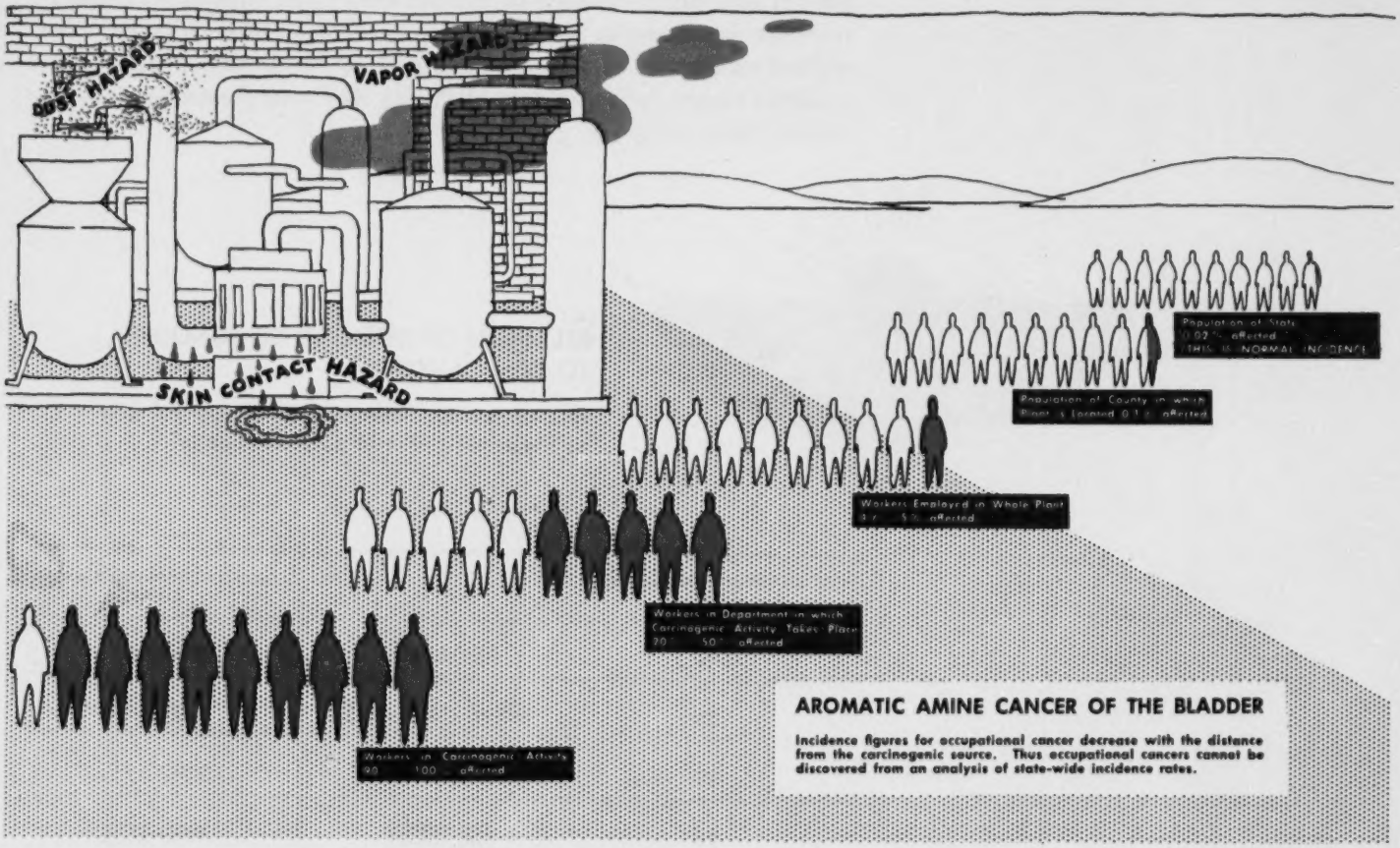


RELATION OF INTENSITY OF SUNLIGHT TO SKIN CANCERS

skin cancer rates and average annual sunlight as percentage of total possible sunlight.

skin cancers per 100,000 population	city	percent of total possible sunlight
140	DALLAS	60%–80%
129	NEW ORLEANS	62%–64%
37	PITTSBURGH	50%–57%
24	DETROIT	40%–25%

aromatic amine cancer The more specialized type of epidemiological analysis results in comparative incidence statistics such as those shown in the chart on cancer of the bladder caused by certain aromatic amines. In this type of study the data are usually collected by the investigator directly from hospital, public health agency, industrial, and other local sources.


DUST HAZARD
VAPOR HAZARD
SKIN CONTACT HAZARD
Population of State
0.02 % affected
THIS IS NORMAL INCIDENCE
Population of County in which
Plant is Located 0.1 % affected
Workers Employed in Whole Plant
3 % 5 % affected
Workers in Department in which
Carcinogenic Activity Takes Place
20 % 50 % affected
Workers in Carcinogenic Activity
90 % 100 % affected
AROMATIC AMINE CANCER OF THE BLADDER
Incidence figures for occupational cancer decrease with the distance from the carcinogenic source. Thus occupational cancers cannot be discovered from an analysis of state-wide incidence rates.

The bladder cancer chart pictures the result of an epidemiological study in a single plant. It differentiates very strongly between those workers most exposed to the carcinogen and those less exposed, and also gives figures on bladder cancer incidence in the county in which the plant exists, and in the state as a whole.

Most of the important data on environmental cancers have been discovered through the careful, scientific use of one or the other of these two types of statistical analysis.

EXPERIMENTATION

Although epidemiological studies of environmental cancers are strongly indicative of the cancer-producing properties of the rays or substances involved, they are not always conclusive. Other factors may be at work in the sample populations studied, though it is not likely that such factors would cause the abnormal incidence figures which often result from careful statistical analyses.

However, conclusive evidence of the cancer-producing qualities of suspected agents is obtained when cancers are elicited in experimental animals after exposure to the carcinogen. This proof of carcinogenicity has been developed for a large number of agents, the great majority of which are products of our industrial environment.

The fact that there are a few animals in which experimental cancers produced by certain specific carcinogens cannot be elicited is very significant. It shows that environmental carcinogens can be as "species-specific," or as selective in their effect upon experimental animals, as are many of the microorganisms which are responsible for the spread of contagious diseases. This selectivity is probably due to differences in metabolization in various animals, or in their reactivity to the specific carcinogen involved.

The species specificity factor makes it obvious that no suspected carcinogen can ever be absolved of dangerous possibilities merely as a result of testing on one animal variety. It may happen that that species is refractory to the particular carcinogen. Several species must be used before an agent's carcinogenic properties can be clearly evaluated. The special anatomical

peculiarities of each species must also be taken into consideration, to assure that proper contact with the carcinogen will be achieved for every type of animal used.

reproduction of occupational cancers in experimental animals

AGENT	ORGAN	SPECIES	
		SUCCESSFUL	UNSUCCESSFUL
SOOT	Skin	Rabbit,* Mouse	
	Lung	Mouse	
ARSENICALS	Skin	Mouse,* Hairless Rat*	Rabbit, Rat
PARAFFIN OIL	Skin	Mouse	
SHALE OIL	Skin	Mouse	
	Lung	Mouse	
PITCH AND TAR	Skin	Mouse, Rat, Rabbit, Dog	Monkey
CRUDE OILS	Skin	Mouse	
ULTRAVIOLET RAYS (SUN)	Skin	Rat, Mouse	Rabbit
ROENTGEN RAYS	Skin	Rabbit, Mouse, Rat	
	Bone	Rabbit	
	Bone Marrow	Mouse	
ANTHRACENE OIL	Skin	Mouse	
DIET DEFICIENCY	Liver	Rat	
RADIOACTIVE SUBSTANCES	Skin	Mouse, Rabbit	
	Bone	Rabbit, Guinea Pig	
	Lung	Mouse	
	Bone Marrow		
LUBRICATING OILS (SOME)	Skin	Mouse	
CREOSOTE	Skin	Mouse	
BENZOL	Bone Marrow	Mouse*	
CHROMATES	Lung		
NICKEL CARBONYL	Lung		
ASBESTOS	Lung	Mouse*	Guinea Pig
TAR FUMES	Lung	Mouse*	
BETA-NAPHTHYLAMINE	Bladder	Dog	Rabbit,* Rat, Mouse
BENZIDINE			Dog

*controversial evidence

CONTROL PROGRAM

Nearly all of the known cancer-causing agents previously listed are widely used in America's industrial processes. Indeed, there is hardly a single industry in which at some point one or more carcinogens are not found, and are potentially dangerous to the people handling them unless proper precautions are taken.

This continued exposure to the environmental cancer danger of workers, technicians, scientists, management personnel, and even the populations of communities near the plants, constitutes an urgent public problem. Important industries using carcinogenic agents are expanding, such as radiation users, dye plants, processors of the various forms of hydrocarbon, metals, solvents, etc.; and new processes involving similar or new types of exposure are constantly being developed. A program of social and technical controls over these hazards must be worked out and put into effect at the earliest possible moment.

An adequate program of control against environmental cancer in American factories and in any American community which is exposed to extrinsic carcinogens should include the following essential points.

technical

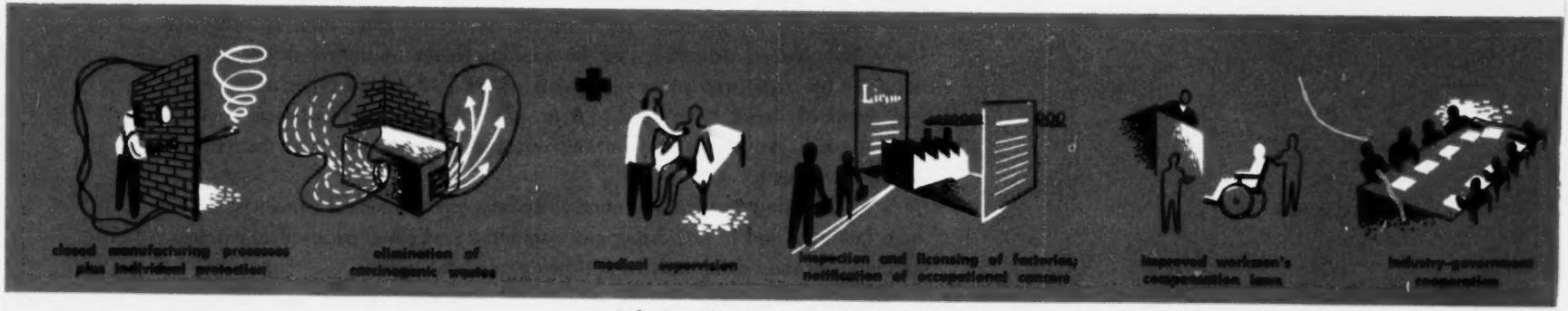
1. Known carcinogenic agents should either be eliminated from industrial, civilian or military use whenever practical and possible, or the degree of prolonged occupational or environmental exposure to them should be depressed to a safe level.

2. Safety procedures should be introduced in all plants where carcinogenic agents are handled. They should include not only protection of the individual workers by enclosing the manufacturing processes, but also protection of the whole plant and of the community at large by preventing the escape of carcinogenic wastes into the atmosphere, the water, or the soil. All new plants should be built with these controls constantly uppermost in the minds of the designers and builders.

3. Adequate protective clothing, respirators, and gloves should be given workers handling carcinogenic substances; separate lockers should be provided for work and street clothes; shower facilities should be installed for all workers; and a thorough indoctrination of exposed workers in the methods

of avoiding exposure to the carcinogens they handle should be made a part of all personnel routines.

4. Periodic and extensive medical supervision of all exposed workers should become standard. These examinations should continue at stated intervals even after the individual worker is no longer in contact with the carcinogen, whether he is still employed in the same plant or not.


closed manufacturing processes plus individual protection
elimination of carcinogenic wastes
medical supervision
inspection and licensing of factories; notification of occupational cancers
improved workmen's compensation laws
industry-government cooperation

social

1. All plants and laboratories manufacturing, handling or using carcinogenic substances should be *licensed* by the States or the Federal Government, and regular inspections should be made to supervise plant control methods, technical, sanitary and medical. Regulations should cover definitions of safe shipping techniques and of proper warning labels for shipping containers.

2. State compensation laws should be amended to cover all aspects of occupational carcinogenesis, for the protection both of workers and of management.

3. All precancerous and cancerous lesions should be added to the list of legally notifiable diseases. Preferably these notifications should be centralized in the hands of State or Federal agencies.

4. Effective cooperation between industry and government should be established through an educational campaign and through conferences. Without this, little or none of the rest of the control program can be successfully initiated or carried out.

CONCLUSION

Environmental carcinogenesis is the newest and one of the most ominous of the end-products of our industrial environment. Though its full scope and extent are still unknown, because it is so new and because the facts are so extremely difficult to obtain, enough is known to make it obvious that extrinsic carcinogens present a very immediate and pressing problem in public and individual health.

It should become one of the most urgent tasks of all medical men, public health officials, labor and management leaders, and members of legislatures, to become familiar with the problems of environmental cancer. They must all work together to combat its causes at the source, before the dread disease spreads to more and more of our people.